



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C12Q 1/68, G01N 33/53</b>		A3	(11) International Publication Number: <b>WO 98/31839</b>
			(43) International Publication Date: <b>23 July 1998 (23.07.98)</b>
(21) International Application Number: <b>PCT/US98/01144</b>		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: <b>21 January 1998 (21.01.98)</b>		Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(30) Priority Data: 08/786,153 21 January 1997 (21.01.97) US 08/804,883 24 February 1997 (24.02.97) US 08/843,623 10 April 1997 (10.04.97) US		(71) Applicant: PRESIDENT AND FELLOWS OF HARVARD COLLEGE [US/US]; 124 Mount Auburn Street, Cambridge, MA 02138-5701 (US).	
(72) Inventor: BAMDAD, Cynthia, C.; 621 Sierra Madre Boulevard, San Marino, CA 91108 (US).		(74) Agent: OYER, Timothy, J.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).	
		(88) Date of publication of the international search report: <b>17 September 1998 (17.09.98)</b>	
(54) Title: ELECTRONIC-PROPERTY PROBING OF BIOLOGICAL MOLECULES AT SURFACES			
(57) Abstract			
<p>A technique for immobilizing biological molecules, in particular nucleic acid strands, is described. Biological molecules immobilized at surfaces can be used in electron-transfer detection techniques in which a binding partner of a biological molecule is brought into proximity of the surface-immobilized biological molecule, an electrical potential created between the two biologically-binding species, and electron transfer through the species determined. Another technique involves immobilizing a biological molecule such as a protein, DNA, etc., at a surface via a self-assembled monolayer, affecting the biological molecule via, for example, biological binding, inducing a change in conformation via a prion, etc., and detecting an electronic property change in the molecule via a change in impedance associated with an electronic circuit addressed by the biological molecule. This technique facilitates combinatorial array detection articles.</p>			

***FOR THE PURPOSES OF INFORMATION ONLY***

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

<b>AL</b>	Albania	<b>ES</b>	Spain	<b>LS</b>	Lesotho	<b>SI</b>	Slovenia
<b>AM</b>	Armenia	<b>FI</b>	Finland	<b>LT</b>	Lithuania	<b>SK</b>	Slovakia
<b>AT</b>	Austria	<b>FR</b>	France	<b>LU</b>	Luxembourg	<b>SN</b>	Senegal
<b>AU</b>	Australia	<b>GA</b>	Gabon	<b>LV</b>	Latvia	<b>SZ</b>	Swaziland
<b>AZ</b>	Azerbaijan	<b>GB</b>	United Kingdom	<b>MC</b>	Monaco	<b>TD</b>	Chad
<b>BA</b>	Bosnia and Herzegovina	<b>GE</b>	Georgia	<b>MD</b>	Republic of Moldova	<b>TG</b>	Togo
<b>BB</b>	Barbados	<b>GH</b>	Ghana	<b>MG</b>	Madagascar	<b>TJ</b>	Tajikistan
<b>BE</b>	Belgium	<b>GN</b>	Guinea	<b>MK</b>	The former Yugoslav Republic of Macedonia	<b>TM</b>	Turkmenistan
<b>BF</b>	Burkina Faso	<b>GR</b>	Greece	<b>ML</b>	Mali	<b>TR</b>	Turkey
<b>BG</b>	Bulgaria	<b>HU</b>	Hungary	<b>MN</b>	Mongolia	<b>TT</b>	Trinidad and Tobago
<b>BJ</b>	Benin	<b>IE</b>	Ireland	<b>MR</b>	Mauritania	<b>UA</b>	Ukraine
<b>BR</b>	Brazil	<b>IL</b>	Israel	<b>MW</b>	Malawi	<b>UG</b>	Uganda
<b>BY</b>	Belarus	<b>IS</b>	Iceland	<b>MX</b>	Mexico	<b>US</b>	United States of America
<b>CA</b>	Canada	<b>IT</b>	Italy	<b>NE</b>	Niger	<b>UZ</b>	Uzbekistan
<b>CF</b>	Central African Republic	<b>JP</b>	Japan	<b>NL</b>	Netherlands	<b>VN</b>	Viet Nam
<b>CG</b>	Congo	<b>KE</b>	Kenya	<b>NO</b>	Norway	<b>YU</b>	Yugoslavia
<b>CH</b>	Switzerland	<b>KG</b>	Kyrgyzstan	<b>NZ</b>	New Zealand	<b>ZW</b>	Zimbabwe
<b>CI</b>	Côte d'Ivoire	<b>KP</b>	Democratic People's Republic of Korea	<b>PL</b>	Poland		
<b>CM</b>	Cameroon	<b>KR</b>	Republic of Korea	<b>PT</b>	Portugal		
<b>CN</b>	China	<b>KZ</b>	Kazakhstan	<b>RO</b>	Romania		
<b>CU</b>	Cuba	<b>LC</b>	Saint Lucia	<b>RU</b>	Russian Federation		
<b>CZ</b>	Czech Republic	<b>LI</b>	Liechtenstein	<b>SD</b>	Sudan		
<b>DE</b>	Germany	<b>LK</b>	Sri Lanka	<b>SE</b>	Sweden		
<b>DK</b>	Denmark	<b>LR</b>	Liberia	<b>SG</b>	Singapore		
<b>EE</b>	Estonia						

# INTERNATIONAL SEARCH REPORT

II. National Application No

PCT/US 98/01144

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 C12Q1/68 G01N33/53

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 22678 A (Baylor College Medicine ; Houston Advanced Res Center (US); Massachusetts) 11 November 1993 see whole document, esp. claims and pages 13, line 9 ff ---	1-12, 19-39
X	CUNNINGHAM B. C. & WELLS J. A.: "Comparison of a structural and a functional epitope" J. Mol. Biol., vol. 234, - 1993 pages 554-563, XP002071221 see esp. results page 555, 2. column and figure 1a --- -/-	40

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance  
"E" earlier document but published on or after the international filing date  
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
"O" document referring to an oral disclosure, use, exhibition or other means  
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

13 July 1998

Date of mailing of the international search report

27/07/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Müller, F

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/01144

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 97 44651 A (AUSTRALIAN MEMBRANE & BIOTECH ;UNIV SYDNEY (AU); HARDING MARGARET) 27 November 1997 see whole doc. esp. page 7 ,line 16 - page 8 ,line 19 and claims ---	1-12,20, 36
P, X	WO 97 41425 A (PENCE INC ;UNIV MCGILL (CA)) 6 November 1997 see whole document, esp. claims and figures ---	1-12,20, 36
A	MURPHY C.J. ET AL.,: "Long-range photoinduced electron transfer through a DNA helix" SCIENCE, vol. 262, - 12 November 1993 pages 1025-1029, XP002071222 cited in the application see esp . page 1028, 3. column ---	1-39
A	SIGAL G. B. ET AL.,: "A self-assembled monolayer for the binding and study of histidine-tagged proteins by surface plasmon resonance" ANAL. CHEM., - 1996 pages 490-497, XP002071235 see the whole document ---	13-18
A	"Kinetic characterization of DNA hybridization using real-time BIA" PHARMACIA BIOSENSOR, APPLICATION NOTES, no. 306, - 1994 XP002071223 see the whole document ---	1-39
A	NILSSON P. ET AL.,: "DNA sequencing with BIA" BIA JOURNAL, vol. 2, no. 2, - 1995 page 25 XP002071224 see the whole document ---	1-39
P, A	US 5 620 850 A (BAMDAD CYNTHIA C ET AL) 15 April 1997 see the whole document ---	13-38
A	NGUYEN J. ET AL.,: "Prion protein peptides induce alpha-helix to beta-sheet conformational transitions" BIOCHEMISTRY, vol. 34, - 1995 pages 4186-44192, XP002071225 see esp. page 4191, last para. -----	40-51

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/01144

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9322678 A	11-11-1993	EP	0638173 A	15-02-1995
		JP	7508831 T	28-09-1995
		US	5653939 A	05-08-1997
WO 9744651 A	27-11-1997	AU	2757897 A	09-12-1997
WO 9741425 A	06-11-1997	AU	2563897 A	19-11-1997
		AU	2563997 A	19-11-1997
		WO	9741424 A	06-11-1997
US 5620850 A	15-04-1997	NONE		

THIS PAGE BLANK (USPTO)